munity and the public of the need to subject beliefs based on limited or local experience to the unblinking objectivity of the scientific method.

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A Scientific Basis for Neurologic Rehabilitation

MEDICAL REHABILITATION in the United States was developed at the end of the 19th century by Deforest Willard, MD, an orthopedic surgeon at the Hospital of the University of Pennsylvania. Major expansions of the field have occurred during wartime, especially World War II, in response to the needs of the many soldiers with limb amputations and traumatic injuries of the nervous system. Rehabilitation medicine stressed the need for patients to develop the maximum attainable degree of self-reliance and psychological acceptance of irreversible impairments. The results were of profound benefit to patients, who might otherwise have returned to lives of helplessness and despair. Rehabilitation medicine also influenced other fields, both within and outside of medicine, to take a more humanistic attitude toward the treatment of patients and a broader view of the capabilities of persons with disabilities. But the clinical and research directions of the field became restricted largely to ameliorating symptoms rather than toward attacks on the pathophysiologic mechanisms of nervous system injury. It was recognized that patients suffering stroke or head injury, and some patients with partial spinal cord injuries, can have dramatic functional recoveries, but the mechanisms underlying these recoveries were not known. Many supposed that functional recovery in the first week or two resulted from the resolution of edema, whereas subsequent recovery was due either to behavioral adaptations or to the assumption of lost functions by spared regions of the nervous system. Axons of the central nervous system were thought to be incapable of regeneration. The control of edema became the subject of many therapeutic trials involving corticosteroids, hypothermia, and other modalities. These showed limited success and, in any case, were deemed in the realm of acute-care medicine and not part of the mission of rehabilitation medicine. Theories of delayed recovery suggested that retraining by passive and active manipulations was the logical therapeutic approach, and this became the focus of most rehabilitation programs, as reflected in the name "Physical Medicine."

The scientific investigative scope of the responses of the nervous system to injury has greatly expanded in the past two decades. This should now bring about a reconsideration of the clinical and academic mission of the field of rehabilitation medicine. The article by Bruce Dobkin, MD, in this issue of the journal reviews the progress that has been made in determining the mechanisms of motor recovery following traumatic or ischemic injury to the central nervous system and in devising methods to enhance this recovery.[1] Dr Dobkin notes that whereas evaluations of traditional models of rehabilitation have not documented superiority of one method over another, the application of rehabilitation techniques based on physiologic or pharmacologic studies in animals has yielded some functional improvements in stroke patients and in patients with incomplete spinal cord injuries. These and other approaches that involve manipulations of the injured nervous system by physical, electrical, or pharmacologic interventions are aimed largely at enhancing the activity of spared or partially injured neuronal pathways. They are important to the mission of rehabilitation because, together with behavioral, educational, and sociologic interventions, they have the potential to lead relatively rapidly to improvements in the quality of life for persons with neurologic disabilities. But it would be a mistake to confine the scientific basis for neurologic rehabilitation to such approaches.

Dobkin's review also mentions recent advances in understanding the factors that prevent the regeneration of in-

jured pathways in the mammalian nervous system and the attempts to enhance regeneration by methods aimed at neutralizing these factors. These avenues of investigation must become an integral part of the scientific basis of rehabilitation medicine. Because they are targeted at a reconstitution of the normal anatomic substrate of neurologic function, they have the potential for a far greater therapeutic benefit and should be viewed as a long-term investment for the field of neurologic rehabilitation.[2] The payoff for these approaches is probably not as far off as most have assumed. More than a decade ago, Aguayo and colleagues in Montreal, Quebec, used modern tract tracing techniques to reemphasize that axons of brain and spinal cord neurons have the capacity to regenerate if given an appropriate environment, such as a graft of peripheral nerve.[3] More recently, this group has demonstrated the ability of optic nerve axons to regenerate for long distances in peripheral nerve bridges and to enter the brain, making electrically active synapses with neurons in the optic tectum.[4] The discovery of molecules on the surfaces of oligodendrocytes (the myelin-producing cells of the central nervous system) that cause the collapse of growing tips of regenerating axons[5] has led directly to experimental procedures to enhance regeneration around a partial spinal cord injury through the use of antibodies specific for those inhibitory molecules.[6] Even the role of glial scarring in inhibiting the regeneration of injured axons is being elucidated with the demonstration that reactive glia secrete proteoglycan molecules that repel growing axons.[7] Enzymatic digestion of these proteoglycans neutralizes their inhibitory action in vitro,[8] a finding that should soon lead to attempts to enhance regeneration in vivo. Finally, experimental success in transplanting fetal nervous system tissue into the mature central nervous system in animals has already led to therapeutic trials in which fetal dopaminergic neurons have been introduced into the brains of patients with Parkinson's disease, with early promising results.[9] There is no evidence that the transplanted cells make synaptic connections with host neurons, and it seems likely that they are acting as a semiglandular source of dopamine rather than as participants in a specific neuronal circuit. Fetal transplants are now being tested in experimental spinal cord injury.[10] There has as yet been no evidence for the recovery of lost functions, but when transplanted into neonatal rats and cats, the fetal spinal cord tissue may enhance the development of locomotion.[11,12]

The failure thus far for axonal regeneration to result in the recovery of lost functions should not lead to an abandonment of attempts to further enhance regeneration. The problem may well be largely with the quantity of regenerating axons, which to date has been a small fraction of those injured. Experiments in lower vertebrates, such as lampreys, where growth-inhibiting factors appear to be absent, suggest that axonal regeneration in the spinal cord is specific with regard to both path finding[13] and synaptic reconnection.[14] Thus, if a greater number of axons could be induced to regenerate in the mammalian central nervous system, they might show a tendency to make appropriate connections, which could lead to the restoration of useful function.

These are exciting developments that are ready for intensive follow-up. The prestige of rehabilitation medicine has long suffered from the impression that its scientific base is weak and that its goals are too restricted. Expansion of the research mission into the areas of morphologic as well as physiologic plasticity in the nervous system is the kind of long-term investment that can rejuvenate the field and attract creative minds to it.

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